400772-02
MRID No.

112701
Schaughnessey No.

EEB Review

BRODIFACOUM, FM?

Secondary poisoning (avian)

1. PESTICIDE:

A. CHEMICAL NAME:

3-(3-[4'-bromo-(1,1'-biphenyl)-4-yl]-1,2,3,4-tetrahydro-1-naphtalenyl)-4-hydroxy-2H-1-benzopyran-2-one

B. COMMON NAME- Brodifacoum.

C. TEST MATERIAL- Unknown, 0.002% Brodifacoum.

2. STUDY TYPE- Secondary toxicity of anticoagulant-killed rodents fed to owls.

3. STUDY IDENTIFICATION:

Mendenhall, V.M. and L.F. Pank. 1980. Secondary poisoning of owls by anticoagulant rodenticides. Wildlife Society Bulletin. 8(4):311-315. USFWS, Denver Wildlife Research Center. no lab ID no. Submitted by Chempar-Lipha Chemicals, 3101 West Custer Ave., Milwaukee, WI 53209. Document no. 5. MRID 400772-02. D175183. Case No. 047415. S331496.

4. REVIEWED BY:

James J. Goodyear, Ph.D.
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Signature: James J Goodyear

Date: April 3, 1993

5. APPROVED BY:

Leslie W. Touart, Ph.D.
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Signature: L. W. Touart

Date:

6. CONCLUSIONS:

The study is scientifically sound but does not fulfil a Guidelines requirements. It was submitted as a Simulated Field Study, Guideline 71-5(a). It is a Secondary poisoning (avian) study (Guideline 70-C-SS) and was reviewed as such. It is a published article. The authors did not do this study to meet FIFRA Guidelines and, therefore, did not specifically address the requirements.

7. RECOMMENDATIONS: N/A.

8. BACKGROUND- It was part of a submission for another anticoagulant.

9. DISCUSSION OF INDIVIDUAL TESTS- N/A.

10. MATERIALS AND METHODS:

A. FORMULATION:

The rats "were fed oat-groat baits containing registered or recommended concentrations of toxicant."

B. PROCEDURES:

The experiment used six rodenticides: Difenacoum, Bromadiolone, Brodifacoum, Diphacinone, Fumarin, and Chlorophacinone.

The rats (Norway rat (*Rattus norwegicus*), Roof rats (*Rattus rattus*), and Polynesian rats (*Rattus exulans*)) were given a free choice of poisoned baits or lab chow for five days. "There were four feeding regimes, in which anticoagulant-killed rats were fed to owls for periods of 1, 3, 6, or 10 days." CO_2 killed rats were then fed to the owls until 20 days after the start of the experiment. The experiments were run in three sections: 1) feeding of dosed rats for 1 and 6 days, 2) 3 and 10 days, and "3) replicate of 2)."

"Toxicants present in rats fed to owls were not quantified. Amounts of toxicants originally consumed by rats are listed in Table 1 and 2, but part of each compound was presumably metabolized and excreted before death."

Coagulant times were measured. Birds were necropsied at the time of death or when sacrificed at day-20. Coagulant times and weights were measured.

C. CONTROLS- Each section had two control owls that were fed undosed rats.

D. RESIDUE SAMPLING OF ANIMALS- None.

E. STATISTICAL ANALYSIS:

The change in the weights of individual owls was analyzed with paired "*t*" tests.

11. REPORTED RESULTS:

Six of seven owls that were fed Brodifacoum-killed rats died. See the authors' "Table 2."

"Hemorrhages occurred throughout the owl carcasses." Several types of internal bleeding occurred. The signs included internal bleeding, bruises from normal activity, and, in one case bleeding from the wound where blood had been sampled 17 days before the test. All the dead birds showed hemorrhaging and heart lesions.

12. STUDY AUTHOR'S CONCLUSIONS/QA MEASURES:

"Birds that died behaved normally until 24 h or less before death, when they became lethargic and stopped eating." The weights at death were not significantly different, but the survivors showed a significant increase in weight.

. . . . . .

"We have demonstrated a potential hazard to avian predators of secondary poisoning by four anticoagulant rodenticides. . . . However, since the protocols differed for treatment of the owl species, further tests using a consistent protocol are needed before we can draw any conclusions on interspecific differences in toxicity.

The effects of anticoagulants on raptors in the field remain to be assessed. However, our results suggest that a potential hazard is likely to exist under some conditions. The amount of toxicant ingested from bait stations by rodents in the field is probably similar to that under our regime (free-choice bioassay of each bait at registered or recommended concentrations); and intensive, large-scale control program also exposes predators to poisoned prey for a number of days. If sufficient prey of affected species were taken by a raptor, secondary poisoning would occur. . . . Susceptibility to anticoagulants can be exacerbated by stress, changes in diet, or increased activity. Minor injury can also increase susceptibility, even if the injury precedes exposure by many days, as in our bird that hemorrhaged at the site where blood had been sampled."

. . . . . .

"The submitter of this study was neither the sponsor of this study nor conducted it, and does not know whether it has been conducted in accordance with 49 CFR Part 160."

13. REVIEWER'S DISCUSSION AND CONCLUSIONS:

A. TEST PROCEDURES:

There was only one owl for each of two dosed regimes (1 and 6 days) and two in repeat trials for the other two regimes (3 and 10 days). Owls are difficult to obtain as experimental laboratory subjects.

The rats were given a free choice of food to approximate the condition that might exist in the wild. Rats in the wild also would be caught by owls after eating the poisoned bait but before death. They would have additional non-metabolized Brodifacoum in their GI tract.

The actual dose of the anticoagulant presented to the owls is unknown. The amount of bait consumed by the rats, time to death, treatment between death and presentation to the owls, and residue analyses of similarly killed rats is not reported. This information in needed to evaluate the conditions that provide for secondary poisoning.

The undosed rats were fed to the surviving owls until 20 days after the start of the experiment. That means that, in the ten day regime, the owls were observed for only ten days. This may not be long enough, but, since the survivors didn't show hemorrhaging, it is sufficient.

The bird that died ate a higher proportion of the intestines (the stomach data was not recorded). This may have contributed to its death because of unmodified poison in the tract. Owls in the wild may not eat every day as did the experimentals, and, thus, may consume all their prey.

Hemorrhages occurred throughout the owl carcasses. Several types of internal bleeding occurred, but the article didn't list them by poison.

B. STATISTICAL ANALYSIS- The change in weight data was not presented.

C. DISCUSSION/RESULTS:

The study does support the conclusions drawn, but it was not done for the registration of Brodifacoum. The conclusions are sufficient to demonstrate that Brodifacoum can kill raptors through secondary poisoning, but it fails to adequately quantify or explain the risk.

D. ADEQUACY OF THE STUDY:

Classification - Supplemental.

Rationale - The dosage is unclear. There was an insufficient number of test subjects.

Repair - None.

Table 2. Secondary toxicity of 6 anticoagulants to barn owls. The full range of doses is shown for the first 3 toxicants; for the last 3 (no effect), only the maximum dose is shown.

Toxicant	Days dosed	Owls		Rats offered		Rats eaten			Intox. signs[b]
		Wt. (g)	Sex	Total wt. (g)	Dose (mg)[a]	Total wt. (g)	Livers	Intestines	
Difenacoum	1	495	M	72	1.74	66	1	0.2	—
	3	430	M	336	6.42	270	3	2.8	—
	3	480	F	189	4.54	125	2.2	3	—
	6	495	M	586	9.81	174	1.2	2.5	H
	10	510	F	1,160	12.54	567	4.8	5.5	H
	10	540	F	595	7.99	477	10	5.8	H
Bromadiolone	1	460	M	118	2.65	52	1	0.8	—
	3	450	M	358	6.60	281	3	3	—
	3	425	M	228	3.96	146	3	2.8	—
	6	490	M	625	11.11	295	5	4	—
	10	540	F	1,106	14.59	576	7.8	4.5	—
	10	635	F	710	9.63	463	8.5	5.2	D(11)
Brodifacoum	1	400	M	71	0.58	67	1	0.5	—
	3	430	M	400	2.50	299	3	2.5	D(8)
	3	475	M	223	1.75	154	3	1.5	D(11)
	6	505	F	580	3.84	370	5.8	3.2	D(9)
	10	470	F	814	3.15	492	6	4.8	D(8)
	10	545	F	558	3.30	368	7	3.8	D(8)
Diphacinone	10	485	F	1,195	11.69	848	10	7.5	—
	10	595	F	575	9.04	490	9.8	7	—
Fumarin	10	520	F	1,137	73.62	751	10	7.5	—
	10	595	F	654	48.89	605	10	8.5	—
Chlorophacinone	10	475	M	1,276	16.07	655	7.2	5.5	—
	10	605	F	712	9.16	576	9	3.5	—

[a] Total toxicant consumed by rat.
[b] Signs of intoxication: — = no signs, H = hemorrhage, survived, D = hemorrhage and death (number indicates day of death from start of dosing).